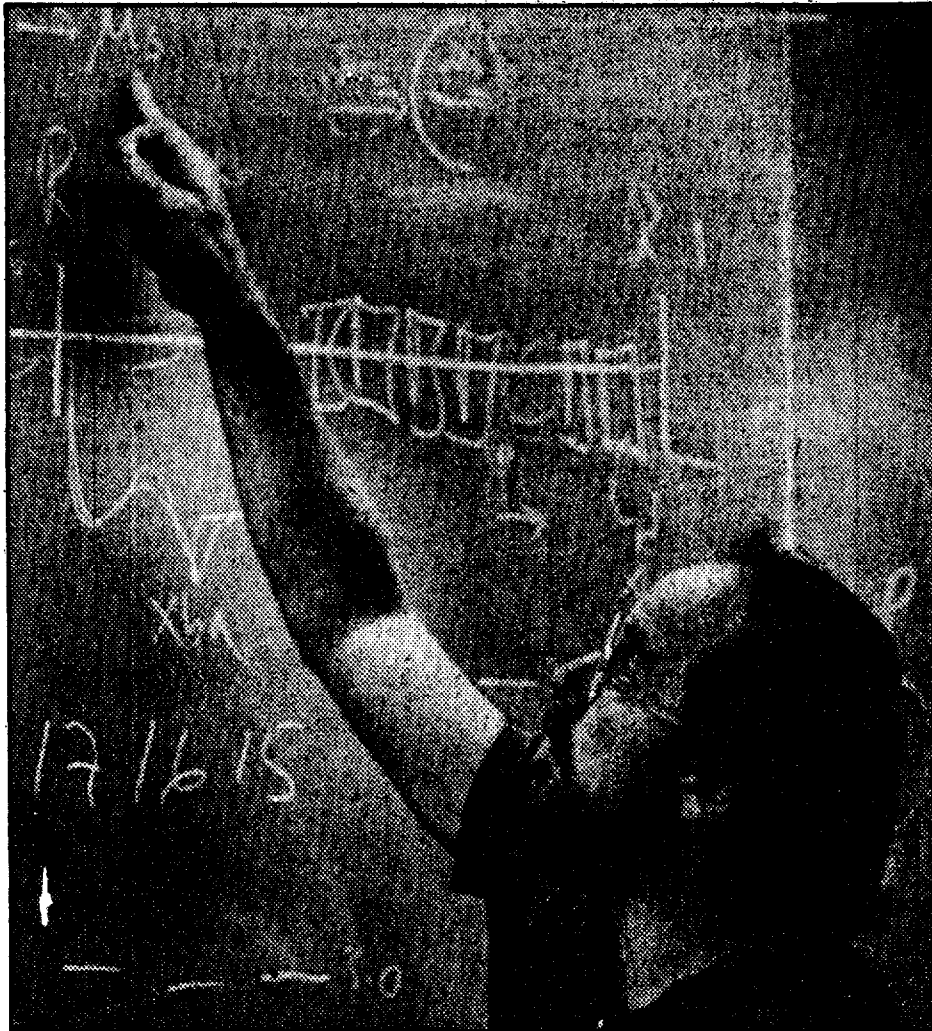


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Dr. David Baltimore works out a problem.

Massachusetts Institute of Technology

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5 Years After the Nobel: Portrait of a Man Obsessed With Science

CAMBRIDGE, Mass.

THE picture on the screen, meaningless to a layman, looked like a row of vertical ink blotches on a dirty gray sheet.

To the dozen or so young men and women clustered in the room, the blots were an unfinished mystery story.

The patterns showed cloned mouse cells that should have been identical. In fact they had grown into two genetically different populations. How? Why?

Orchestrating the discussion was a bearded man in his early 40's, smoking a pipe, wearing metal-rimmed glasses, a dark red sport shirt and suntan pants. His young colleagues addressed him as "David." He is known to the world at large as Dr. David Baltimore, American Cancer Society Professor of Microbiology at M.I.T., co-winner of a Nobel Prize and one of the most brilliant and inventive minds in modern American science.

As he and the young scientists tried to make sense of those mouse cells, Dr. Baltimore's comments were sparse but telling, terminating one line of investigation, encouraging another.

"I don't think it's going to be worthwhile to drive that into the ground," he said at one point.

"Good, very good," he said almost inaudibly at another.

One research worker said two specimens seemed to be identical.

"No," Dr. Baltimore said quickly, "they are reversed."

The meeting was informal, conducted at lunchtime with sandwiches from paper bags. Excitement and concentration seemed to wax and wane with the discussion.

Dr. Baltimore sat at the side, only occasionally asking a question or rising to go to the chalkboard. But the speakers seemed to be directing their words as much to him as to the rest of the group.

The young M.I.T. scientists were seeking ways to harness this particular paradox — to make it reveal an underlying truth about the immune defense system of humans and animals.

The cells were precursors of those that produce the disease-fighting substances called antibodies. The experiments, still in progress, might explain something important about the development of these indispensable cells.

Dr. Baltimore's research style and the way he imparts it to a new generation reveal something of the creative genius of modern biology, something of the fire that has kindled a revolution in human understanding of the chemistry of life on earth.

"I think it's partly a habit of mind," he told a visitor. "It involves a kind of obsessiveness. Unless you are obsessed with scientific questions you are not going to get anywhere with them."

Also needed, he says, is a talent for thinking a logical train of experiments through to its long-term consequences. The layman's perception is often that of a scientist working doggedly, in lonely dedication, toward some distant goal. The reality, Dr. Baltimore says, is that a scientist must learn to find the path of least resistance through a maze of scientific unknowns, choosing the experiments that are ripe to be done, even backing off from a tough problem until some new insight or new technique softens it up.

He once backed off from an impasse in virus research for 17 years and then picked

it up again when a new development made the question ripe for solving. The lapse had continued to bother him over the years until he ended it.

Brilliance in scientific research is not a simple talent, nor is it simply explained. The obsessive urge to find answers is clearly a part of it, as is the talent for choosing the right questions. Dr. Baltimore says he wakes up in the morning thinking — and assumes everyone else does, too. There were times in his early career, notably at Rockefeller University, when his waking hours were science and nothing but science; meals were the only breaks in the work, and even these functioned as opportunities to discuss science with colleagues.

Once in the Vietnam War years he halted important research for a week in protest against the invasion of Cambodia, all the while feeling the compulsion to make the protest but also the agony over the delay in his experiments.

The ability to devise fruitful experiments is largely a learned talent, he says, that can be passed on to students. The meeting of his laboratory group showed that process at work.

Today Dr. Baltimore's creative role is mainly that of a catalyst, directing research rather than doing it himself. But his talents

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Obsession of a Prize-Winning Scientist

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and style put an imprint on the work. He is a man of great energy and, some of his students say, a library of valuable information on many aspects of molecular biology.

His current obsessions embrace some of the key fields in molecular biology: study of how viruses reproduce and how some of them transform normal cells to a state like cancer; study of immunology, the internal defense system that tells friend from foe and fights back against invasion by germs and other intruders in the living body.

Central to much of the work is the sometimes controversial recombinant DNA technology. With it, scientists can make limitless copies of the pieces of deoxyribonucleic acid that serve as the genes of all forms of life; can snip and splice and rearrange genes from any species; can combine genetic material from man and mouse, and can grow human genes in bacteria.

Mathematics Came Easy

Dr. Baltimore was introduced to the real obsessions of science as a high school student in the middle 1950's. Mathematics and related fields came easy to him, he recalls, but fascination began to germinate at a summer session for high school students at the Jackson Laboratory in Bar Harbor, Me. The young visitors to the famous laboratory listened to lectures, did some research projects and discussed biology with experts.

Although Dr. Baltimore did not decide on a career in science until he was about halfway through his undergraduate studies at Swarthmore College, he now recognizes the Jackson laboratory experience as a key determinant.

The person he remembers as the "guru" of his group was Howard M. Temin, now of the McArdle Laboratory at the University of Wisconsin.

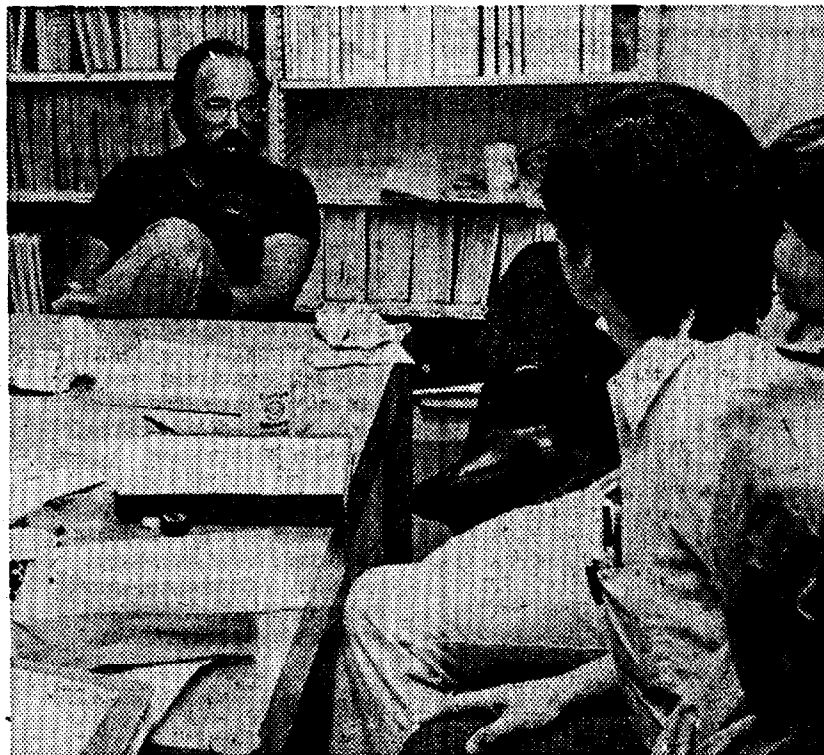
The two never worked together after that summer. Neither had more than a passing knowledge of what the other was up to as their careers evolved in the next decade and a half. Their habits of mind, or at least their scientific styles, grew to be far different.

Yet, in one of the ironies of modern science, their research paths converged until, in 1970, they each, independently and unknown to the other, did almost the same experiments with viruses and thereby demolished what many considered a central dogma of modern molecular biology. Five years later they and Dr. Renato Dulbecco, one of the towering figures of modern biology, were awarded the Nobel Prize.

Looking Like Dr. Ehrlich

A photograph of Dr. Baltimore shaking hands with the King of Sweden at the Nobel Prize ceremonies that fall shows the young American scientist dressed in formal costume and looking a little like Paul Muni playing Dr. Paul Ehrlich in the 1930's movie "Dr. Ehrlich's Magic Bullet." The film was made approximately the year Dr. Baltimore was born.

In the research cited by the Nobel committee, Drs. Temin and Baltimore had identified a special class of enzymes through which certain viruses could subvert the genetic machinery of the cells they infected.



Massachusetts Institute of Technology

Dr. Baltimore and his research staff meet regularly at a weekly "brown bag" lunch conference.

The two closely related master chemicals of heredity are DNA and ribonucleic acid (RNA). The arrangement of chemical subunits in the DNA serves as the genetic code spelling out each message of heredity. One of the key functions of RNA is to form a copy of the DNA and use this as the blueprint for the production of the specific protein coded for by the gene.

It had been almost universally assumed that the flow of information was always from a nucleic acid to protein. Some thought it always from DNA to RNA to protein. That concept left scientists puzzled over the ability of some of the viruses that contained RNA instead of DNA to transform the very nature of the cells they infected — to make them cancerous. Somehow, they reasoned, the virus RNA must be leaving its message permanently in the DNA of the infected cell.

The discovery of the enzymes now known as reverse transcriptases solved that puzzle.

Such an enzyme was found by Dr. Tamin in a virus that causes cancer in chickens. Dr. Baltimore found his in a virus that causes leukemia in mice. It soon became clear that RNA-containing viruses known to cause cancer in animals had these subversive enzymes while other viruses did not. Their existence, denied on theoretical grounds for years, proved to be a general phenomenon. Students since then have confirmed its profound importance.

Working closely with about 20 younger scientists today, Dr. Baltimore says he can see in some of them the possibility of creative greatness, although he adds quickly that creativity really defies prediction. Some scientists plug along for decades, then abruptly blossom into brilliant productivity. Others, seemingly racing ahead in the throes of genius, suddenly fade

and lose the fire. Some concentrate narrowly. Others leap at creative opportunity where they perceive it.

Dr. Baltimore likes to be in the competitive forefront of a field and does not leave when the field becomes crowded with research workers following the current fashion. He has sometimes been criticized for his zeal in leaping into highly active fields.

The scientist credits association with many brilliant workers for helping shape his talents. Notable among these has been Dr. Alice Huang, a microbiologist at Harvard Medical School, an early collaborator on virus research and now his wife.

About six months after he had joined the laboratory of Richard Franklin at Rockefeller Institute (now University) in the early 1960's, he was doing significant work at the forefront of the science of that day. He says he does not know just how this happened, except, that he was always allowed to follow his own creative path.

But there were older scientists at that time too who could see talent for creativity taking shape.

"There are times in the development of a field of knowledge when the ground for the next major development is laid," said Dr. Igor Tamm of Rockefeller on an important occasion in 1964.

"David's teachers and associates have all been impressed with his broad grasp of concepts and the integrative quality of his mind," he continued. "I therefore think that David has ample qualifications not only for a productive life in research, but also for a rewarding life in teaching. I expect that his lively interests in science will fire enthusiasm in others; that his insights will illuminate many."

The occasion was the presentation of David Baltimore for the Ph.D. degree, at the beginning of a creative career whose dimensions are still unfolding.